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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
FALK, ANNE MARIE	

ART UNIT	PAPER NUMBER
1632	

DATE MAILED: 10/29/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Advisory Action	Application No.	Applicant(s)	
	09/656,935	BLUSZTAJN ET AL.	
	Examin r	Art Unit	
	Anne-Marie Falk, Ph.D.	1632	

--The MAILING DATE of this communication appears on the cover sheet with the correspond nce address --

THE REPLY FILED 11 September 2003 FAILS TO PLACE THIS APPLICATION IN CONDITION FOR ALLOWANCE. Therefore, further action by the applicant is required to avoid abandonment of this application. A proper reply to a final rejection under 37 CFR 1.113 may only be either: (1) a timely filed amendment which places the application in condition for allowance; (2) a timely filed Notice of Appeal (with appeal fee); or (3) a timely filed Request for Continued Examination (RCE) in compliance with 37 CFR 1.114.

PERIOD FOR REPLY [check either a) or b)]

a) ☐ The period for reply expires _____months from the mailing date of the final rejection.

b) ☐ The period for reply expires on: (1) the mailing date of this Advisory Action, or (2) the date set forth in the final rejection, whichever is later. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of the final rejection.
ONLY CHECK THIS BOX WHEN THE FIRST REPLY WAS FILED WITHIN TWO MONTHS OF THE FINAL REJECTION. See MPEP 706.07(f).

Extensions of time may be obtained under 37 CFR 1.136(a). The date on which the petition under 37 CFR 1.136(a) and the appropriate extension fee have been filed is the date for purposes of determining the period of extension and the corresponding amount of the fee. The appropriate extension fee under 37 CFR 1.17(a) is calculated from: (1) the expiration date of the shortened statutory period for reply originally set in the final Office action; or (2) as set forth in (b) above, if checked. Any reply received by the Office later than three months after the mailing date of the final rejection, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

1. ☒ A Notice of Appeal was filed on *11 September 2003*. Appellant's Brief must be filed within the period set forth in 37 CFR 1.192(a), or any extension thereof (37 CFR 1.191(d)), to avoid dismissal of the appeal.

2. ☒ The proposed amendment(s) will not be entered because:

   (a) ☒ they raise new issues that would require further consideration and/or search (see NOTE below);

   (b) ☐ they raise the issue of new matter (see Note below);

   (c) ☒ they are not deemed to place the application in better form for appeal by materially reducing or simplifying the issues for appeal; and/or

   (d) ☐ they present additional claims without canceling a corresponding number of finally rejected claims.

   NOTE: *See Continuation Sheet*.

3. ☐ Applicant's reply has overcome the following rejection(s): _____.

4. ☐ Newly proposed or amended claim(s) _____ would be allowable if submitted in a separate, timely filed amendment canceling the non-allowable claim(s).

5. ☒ The a)☐ affidavit, b)☐ exhibit, or c)☒ request for reconsideration has been considered but does NOT place the application in condition for allowance because: *See Continuation Sheet*.

6. ☐ The affidavit or exhibit will NOT be considered because it is not directed SOLELY to issues which were newly raised by the Examiner in the final rejection.

7. ☒ For purposes of Appeal, the proposed amendment(s) a)☒ will not be entered or b)☐ will be entered and an explanation of how the new or amended claims would be rejected is provided below or appended.

   The status of the claim(s) is (or will be) as follows:

   Claim(s) allowed: _____.

   Claim(s) objected to: _____.

   Claim(s) rejected: *7,9,11,12,14 and 17*.

   Claim(s) withdrawn from consideration: _____.

8. ☐ The proposed drawing correction filed on _____ is a)☐ approved or b)☐ disapproved by the Examiner.

9. ☐ Note the attached Information Disclosure Statement(s)(PTO-1449) Paper No(s). _____.

10. ☐ Other: _____

Anne-Marie Falk

Anne-Marie Falk, Ph.D.
Primary Examiner
Art Unit: 1632

Continuation of 2. NOTE:

Newly proposed Claim 18 and the proposed amendments to Claims 7, 11, and 12 would require new grounds of rejection. For example, Claim 18 would require a new rejection under 112, first paragraph for lack of enablement and under 112, second paragraph for indefiniteness with regard to "preventing brain function" as it is unclear how inducing differentiation of progenitor cells into cholinergic neurons would prevent brain function. Newly proposed Claim 18 would require a new ground of rejection under 35 U.S.C. 112, second paragraph, as the preamble is in conflict with the effect achieved by the method. Claim 18 raises new issues that would require further consideration as the claim recites "preventing brain function and/or memory loss." This is a new claim limitation not recited in the examined claims. The proposed amendment to Claims 7, 11, and 12 would remove the phrase "in need of same" thereby broadening the scope of the claims. As amended the claims would cover the use of healthy patients. This raises new issues that would require further consideration.

Continuation of 5. The request for reconsideration has been considered but does NOT place the application in condition for allowance because:

With regard to the rejection under 35 U.S.C. 112, first paragraph, Applicants arguments are limited to the assertion that administration of BMP-9 can be used to **induce upregulation** of the genes associated with the cholinergic phenotype (pages 4-8). Thus, Applicants arguments are limited to Claims 11 and 12. However, Claims 7, 9, 17, and proposed new Claim 18 are directed to **differentiating progenitor cells** into cholinergic neurons in a patient. These claims do not involve induced upregulation of genes.

With regard to Claims 11 and 12, Applicants assert that BMP-9 induced upregulation of the genes associated with the cholinergic phenotype would necessarily translate into a prediction that BMP-9 would

upregulate these genes in adult mouse and human tissue. However, no support is offered for this assertion. For reasons of record, the effect of BMP-9 within the brain of a diseased animal, with an ongoing pathological process, is unpredictable, particularly given that one of skill in the art would not expect that upregulation of genes within existing neurons would be sufficient to replace the connections lost by cholinergic neurons that have already degenerated.

At page 8, paragraph 1 of the response, Applicants argue that "while the cause and effect of AD may not be completely clear, the direct result of degeneration of cholinergic neurons is quite predictable, as is the result of **prevention of cholinergic neuron degeneration**" (emphasis added). Only Claim 14 recites preventing degeneration (of motor neurons). However, none of the other claims are directed to **preventing degeneration** of cholinergic neurons. On the contrary, Claims 7, 9, 17, and proposed new Claim 18 are directed to **generating new cholinergic neurons** from progenitor cells. There is nothing in the specification to suggest that these new neurons would form appropriate synapses or that they would be located in the appropriate region within the neural network. The specification does not provide specific guidance with regard to the location of neuronal progenitor cells within the adult brain, such that one of skill in the art could reasonably expect these newly generated cholinergic neurons to integrate into a functioning neural network, and particularly within those gaps in the neural network where cholinergic neurons have been lost. In AD, the pathological process results in the loss of cholinergic enzymes. Since this process is not inhibited by the instantly claimed methods, the newly formed cholinergic neurons, if they arise at all in the adult, are subject to the same fate as the degenerating neurons.

With regard to the rejection of Claims 9 and 17 under 35 U.S.C. 112, second paragraph, Applicants arguments are moot in view of the fact that the proposed amendment has not been entered for the reasons discussed herein above.

Thus, the claims remain rejected for reasons of record. All grounds of rejection are maintained.